Reviewer's report

Title: Common Genetic Variants on Chromosome 9p21 Are Associated with Myocardial Infarction and Type 2 Diabetes in an Italian Population.

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Reviewer: Harald Goring

Reviewer's report:

This manuscript describes the results from a 2 candidate SNP association study with myocardial infarction (MI) and with type 2 diabetes mellitus (T2DM) in an Italian sample. These 2 SNPs were chosen because they had previously been reported to be associated with coronary artery disease (CAD) and T2DM in the European PROCARDIS consortium. The findings reported here are in agreement with the PROCARDIS study results, i.e. one SNP (rs2891168) was associated with MI but not T2DM, and the other SNP (rs10811661) was associated with T2DM but not MI. This is also of interest because both SNPs are located in a locus of chromosome 9 that was identified as harboring genetic risk factors for both diseases. Hence, given the frequent co-occurrence of both disorders, one hypothesis is that it is the same polymorphisms that influence risk for both diseases, and another hypothesis is that the variants are different. With respect to these 2 particular SNPs, they are each associated only with one of the two diseases.

Major points:

It is difficult to assess whether the finding is novel and significant because the authors only explicitly provide results on these 2 SNPs from the PROCARDIS consortium. Based on Figure 2, it appears that the joint results from this investigation and the PROCARDIS dataset are quite convincing with regard to the association for these 2 SNPs, but no p-values are provided. Certainly the evidence from this study alone is very marginal (p-values of 0.03 with MI and 0.02 with T2DM, and similar results contrasting individuals with both conditions with groups of individuals suffering only from one of the two diseases). The authors should explicitly summarize the findings regarding these 2 specific SNPs from other studies, such as various genome-wide association studies. Simply referring to the region on chromosome 9 is too vague and not precise enough. Without going on a literature review, a reader will not be able to assess whether the findings are truly convincing or not, and whether they are novel and important or merely confirm of what is already well known.

The authors should state explicitly where the samples come from. Simply referring to earlier manuscript is not sufficient. This information is valuable for assessing whether or not differences in genetic constitution between the various case groups and controls may be a concern or not.
Minor points:

“a [...] power calculation indicated [...] 80% poser to highlight at least a 30% genetic risk for diabetes …”: 30% genetic risk does not appear to be the appropriate terminology.

“The susceptibility effects of rs2891168 on MI […] in the Italian population is less strong, partially because the sample is smaller”: This makes no sense. The variance of the estimate is influenced by sample size, but the expected value is not.

Regarding Figures 1 and 2: “Solid squares centered on the OR [are] scaled in proportion to sample size”: Why are the sample sizes different for the 2 SNPs? The number of individuals in the 3 case groups are essentially the same.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.